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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/498,046	02/04/2000	Sabine Neirynck	VIB-08	8244

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WELSH & KATZ, LTD
120 S RIVERSIDE PLAZA
22ND FLOOR
CHICAGO, IL 60606

EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	
MAIL DATE	**DELIVERY MODE**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/498,046	NEIRYNCK ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-32,34 and 36-57* is/are pending in the application.

4a) Of the above claim(s) *42-45 and 47-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,27,36-38,40,41,46 and 54-57* is/are rejected.

7)☒ Claim(s) *28-32,34,39,52 and 53* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date ~~4/23/07~~ 4/30/07 /SBC 6/25/07
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and response filed April 11, 2007 is acknowledged and entered. Claims 26-32, 34 and 36-57 are pending. Claims 42-45 and 47-51 remain withdrawn from consideration being drawn to non-elected subject matter. Claims 28-32, 34, 39, 52 and 53 are under examination.

2. The rejection of claims 34, 39, 52 and 53 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of Applicant's amendment.

Claims Summary

3. The claims are drawn to an immunogenic composition comprising a fusion product. The fusion product is comprised of one of the following constructs:

- An immunogenic extracellular part of an M2 membrane protein of a human influenza A virus and a heterologous presenting carrier.
- An immunogenic extracellular part of an NB protein of a human influenza B virus and a heterologous presenting carrier.
- An immunogenic extracellular part of a CM2 protein of a human influenza C virus and a heterologous presenting carrier.

The presenting carrier is a peptide or polypeptide. Specifically, the peptide or polypeptide is a hepatitis B core protein, C3d, polypeptides comprising multiple copies of C3d, tetanus toxin fragment C or yeast Ty particles. In another embodiment, the carrier is a non-peptidic structure. The fusion product is in an isolated form. The fusion product may also be anchored in the

membrane of an acceptor cell expressing the fusion product. The fusion product is part of a lipid bilayer or cell wall. The amino acid sequence of the entire extracellular domain is SEQ ID NO: 1, 2 or 3.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26, 27, 36, 37, 38, 40, 41, 46 and 54-56 remain rejected under 35 U.S.C. 102(b) as being anticipated by Kurtz *et al.* (U.S. Patent 5,691,189, "Kurtz"). The claims are summarized above. Kurtz discloses the expression of influenza A virus M2 protein from *S. cerevisiae* cells (abstract). *S. cerevisiae* cells are a heterologous presenting carrier. The M2 protein is expected to be fused to the cells since the M2 gene is engineered to be expressed by the cells (col. 3, lines 25-31). The M2 protein is a protein having at least the smallest portion of the full-length wild-type M2 protein that results in growth impairment in *S. cerevisiae* cells (col. 3, lines 32-36). Kurtz's M2 protein is expected to contain an immunogenic extracellular part of the M2 because the protein is disclosed to associate into tetramers to form ion channels (col. 1, lines 37-42). Since Kurtz teaches that one of the uses for the M2 protein expressed on yeast cells is in an assay to detect modulators of the M2 ion channel, the extracellular part of M2 must be expressed in Kurtz's construct. Kurtz discloses that the inhibitors of the M2 channel would be effective antiviral agents (col. 1, lines 51-52).

Kurtz does not mention whether the influenza A is human. Kurtz's SEQ ID NO: 3 contains Applicant's SEQ ID NO: 1,which is human. Since the sequences are identical, Kurtz's composition must be comprised of an immunogenic extracellular part of an M2 of a human influenza A virus. Although Kurtz does not disclose the yeast cell/M2 constructs as compositions to be administered to humans or other animal species, the claims are drawn to products. The intended uses of the products are not given patentable weight. The structural limitations of the claims have been met by the teachings of Kurtz.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(*New Rejection*) Claims 26, 27, 36, 37, 38, 40, 41, 46 and 54-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurtz in view of Sunstrom *et al.* (*J. Membrane Biol.* 1996, 150:127-132, "Sunstrom"). The claims and the teachings of Kurtz are summarized above. Although Kurtz does not disclose the use of the human influenza B virus NB protein, Sunstrom discloses that influenza B virus NB protein forms ion channels (abstract). (Influenza B viruses are known to infect humans only, thus the NB protein from influenza B must be a human protein.) It would have been obvious to substitute the NB protein of Sunstrom into Kurtz's *S. cerevisiae* cells. Kurtz teaches that one of the uses for the M2 protein expressed on yeast cells is in an assay to detect modulators of the M2 ion channel, thus identifying inhibitors of the M2

channel as effective antiviral agents (Kurtz, col. 1, lines 51-52). One would have been motivated to substitute the ion channel forming protein NB of influenza B virus for the M2 channel in order to identify inhibitors of the influenza B ion channel, NB. One would have had a reasonable expectation of success that the ion channel of the influenza B virus would have been successfully expressed from Kurtz's *S. cerevisiae* cells because the ion channel protein of influenza A virus (M2) was successfully expressed from *S. cerevisiae* cells. Therefore, the embodiment of the influenza B virus NB protein would have been obvious to one of ordinary skill in the art at the time the instant invention was made.

Response to Arguments

6. Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments regarding the 102 and 103 rejections are primarily directed to the following:

- Applicant argues that Kurtz's expression of the M2 protein in yeast cells does not anticipate the claimed invention. Applicant notes that the claims require a fusion product, which means that the recited parts of the fusion product are chemically linked together. Applicant points to Exhibit A, which shows a search of the USPTO database of issued patents that recite the term "fusion product". Applicant argues that the meaning of the term "fusion product" is recognized in the art and understood. Applicant argues that the Kurtz disclosure does not teach the expressed protein being linked to a carrier as fusion product.

- In response to Applicant's arguments, the Office is aware of meaning of "fusion product", and also recognizes that Kurtz does not use the term "fusion product". However, the missing term does not alter Kurtz's construct of a yeast cell expressing an M2 protein. The M2 protein is expected to be fused to the cells since **the M2 gene is engineered to be expressed by the cells** (col. 3, lines 25-31). The yeast cell expresses the M2 protein through its normal transcription and translation mechanisms, and the M2 protein acts as an ion channel (col. 1, lines 57-61, and col. 2, lines 15-19). It is clear that the M2 protein remains fused to the cell, since a secreted M2 ion channel would not be effective for Kurtz's construct.

- Applicant argues that the product of Kurtz does not potentiate the immunogenicity of the product. Applicant asserts that the full-length M2 protein is inserted in Kurtz into the plasma membrane of the yeast cells. Applicant argues that because yeast cells have a cell wall external to the plasma membrane, the M2 protein and its extracellular part are not directly exposed to the immune system by the yeast cells. Applicant concludes that the Kurtz construct does not present the M2 protein because the M2 protein is not exposed to the immune system.

  - In response to Applicant's arguments, the M2 protein is not merely "inserted" into the yeast cell. The M2 protein is expected to be fused to the cell since the M2 gene is engineered to be expressed by the cell (col. 3, lines 25-31). With regard to the presence of the M2 protein in the plasma membrane versus the cell wall, the instant claims recite, "the fusion product is anchored in the membrane of an acceptor cell expressing the fusion product", see claim 37, for example. It is

unclear how Applicant's argument applies because Applicant's own invention allows the M2 protein to be in the plasma membrane (which has a cell wall external to the membrane). If Applicant's argument is valid, then Applicant's own construct is not presented to the immune system and therefore is not capable of potentiation. Regardless, Kurtz discloses the M2 protein as an ion channel. Ion channels are anchored in the plasma membrane and facilitate ion exchange with the yeast cell's outer environment. Thus, the M2 protein is not being expressed and stored away under the cell wall, but it is expressed and functions as a channel. Therefore, the yeast cells are still considered by the Office to be heterologous presenting carriers of the M2 protein, capable of immunopotentiation. The claims, as broadly written, remain anticipated and obvious in view of the references of record.

Conclusion

7. Claims 28-32, 34, 39, 52 and 53 are objected to for depending from rejected claims.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 6-18-2007
Primary Examiner, TC1600